UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/594,515	09/28/2006	Robin Polt	295123US96PCT	1817

22850 7590 01/15/2009

OBLON, SPIVAK, MCCLELLAND MAIER & NEUSTADT, P.C.
1940 DUKE STREET
ALEXANDRIA, VA 22314

EXAMINER	
RUSSEL, JEFFREY E	

ART UNIT	PAPER NUMBER
1654	

NOTIFICATION DATE	DELIVERY MODE
01/15/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

patentdocket@oblon.com
oblonpat@oblon.com
jgardner@oblon.com

Office Action Summary	Application No.	Applicant(s)	
	10/594,515	POLT ET AL.	
	Examiner	Art Unit	
	Jeffrey E. Russel	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 November 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-37* is/are pending in the application.

4a) Of the above claim(s) *3-5,15,19 and 21* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,6-14,16-18,20 and 22-37* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *28 September 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *20060928*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

1. Applicant's election of the species in which (A) the N-terminal sequence is Y-t-G-F-L-G-G; (b) one serine residue is glycosylated; and (C) the glycosyl unit has two saccharide units; in the reply filed on November 18, 2008 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 3-5, 15, 19, and 21 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected species, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on November 18, 2008.

2. The Sequence Listing filed December 17, 2007 is approved.

3. The abstract of the disclosure is objected to because at line 2, "an" should be changed to "and". Correction is required. See MPEP § 608.01(b).

4. The disclosure is objected to because of the following informalities: At page 11, line 26, "dimyristoylphosphatidylcholine" is misspelled. Appropriate correction is required.

5. Claim 6 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. There is no antecedent basis in the claims for the phrase "the N-terminal sequence" in claim 6. It is possible that claim 6 should instead depend from claim 2.

6. Claims 16-18 and 35-37 are objected to because of the following informalities: In each of claims 16-18, "glycosylated" is misspelled. In each of claims 35-37, "of" should be inserted before "Claim 1". Appropriate correction is required.

7. Instant claims 1, 2, 6-14, 16-18, 20, and 22-37 are deemed not to be entitled under 35 U.S.C. 119(e) to the benefit of the filing dates of provisional applications 60/557,740,

60/583,257, or 60/641,492 because the provisional applications, under the test of 35 U.S.C. 112, first paragraph, do not disclose, e.g., amphipathic glycopeptides in general which do not comprise specific N-terminal opioid message sequences, specific C-terminal address sequences, and specific linker sequences between the message sequences and the linker sequences; do not disclose amphipathic glycopeptides having any size which is 9 amino acids or greater; and do not disclose amphipathic glycopeptides in which any number of any type of amino acid residue is glycosylated in any manner. See MPEP 201.11(I).

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

9. Claims 1, 9-12,16-18, 22-28, 30, 32, and 34 are rejected under 35 U.S.C. 102(b) as being anticipated by the Bulet et al article (Eur. J. Biochem., Vol. 238, pages 64-69). The Bulet et al article teaches drosocin, which is a 19-amino acid residue peptide which is glycosylated with a disaccharide at Thr^{11}. After synthesis, the drosocin is dissolved in water. CD spectra of drosocin in water in the absence of a lipid bilayer shows a peptide secondary structure without structural preferences, i.e. is non-helical. See, e.g., page 65, column 1; page 66, paragraph bridging columns 1 and 2; and Figures 2 and 4. The drosocin of the Bulet et al article is an amphipathic peptide because it comprises both hydrophilic and hydrophobic amino acid residues. See Applicants' definition of "amphipathic" at page 6, last paragraph, lines 3-6. With respect to instant claims 9, 11, 29, and 30, in view of the similarity in structure and CD spectra in water

between the drosocin of the Bulet et al article and Applicants' claimed glycopeptides, inherently the drosocin of the Bulet et al article will adopt a helical conformation in the presence of a lipid bilayer, will show a % helicity as measured by circular dichroism in water and in the presence of a lipid bilayer, and will cross the blood-brain barrier, to the same extent claimed by Applicants. Given the scope of potential message sequences, address sequences, and subjects embraced by Applicants' claims, inherently an N-terminal portion of the drosocin of the Bulet et al article will function as a non-opioid message sequence for at least one subject, inherently a C-terminal portion of the drosocin of the Bulet et al article will function as an address sequence for at least one subject, and the remaining portion of the drosocin of the Bulet et al article will correspond to Applicants' linker sequence. Sufficient evidence of similarity is deemed to be present between the drosocin of the Bulet et al article and Applicants' claimed glycopeptides to shift the burden to Applicants to provide evidence that the claimed glycopeptides are unobviously different than the drosocin of the Bulet et al article. With respect to instant claim 34, the water in which the drosocin of the Bulet et al article is dissolved corresponds to Applicants' pharmaceutically acceptable carrier and/or excipient. Note that an intended use limitation, i.e. "pharmaceutical", does not impart patentability to a product claim were the product is otherwise anticipated by the prior art.

10. Claims 1, 9-14, 16-18, 20, 28-30, 32, and 34 are rejected under 35 U.S.C. 102(b) as being anticipated by Konig et al (U.S. Patent No. 5,091,367). Konig et al teach gonadoliberin analogs comprising one or two glycosylated serine residues. Glycosylation can be with monosaccharides such as glucose, and with disaccharides and trisaccharides. One species is an analog comprising one serine glucoside residue. The analogs are used pharmaceutically in combination with a

pharmaceutically acceptable carrier. See, e.g., formula (I); column 3, lines 18-47; Table 1, second entry; and claims 4 and 9-11. The analogs of Konig et al are amphipathic peptides because they comprises both hydrophilic (e.g., non-glycosylated Ser and Arg) and hydrophobic (e.g., Tyr and Leu) amino acid residues. See Applicants' definition of "amphipathic" at page 6, last paragraph, lines 3-6. With respect to instant claims 9-11, 29, and 30, in view of the similarity in structure between the analogs of Konig et al and Applicants' claimed glycopeptides, inherently the analogs of Konig et al will adopt a helical conformation in the presence of a lipid bilayer, will be substantially non-helical in water in the absence of a lipid bilayer, will show a % helicity as measured by circular dichroism in water and in the presence of a lipid bilayer, and will cross the blood-brain barrier, to the same extent claimed by Applicants. Given the scope of potential message sequences, address sequences, and subjects embraced by Applicants' claims, inherently an N-terminal portion of the analogs of Konig et al will function as a message sequence for at least one subject, inherently a C-terminal portion of the analogs of Konig et al will function as an address sequence for at least one subject, and the remaining portion of the analogs of Konig et al will correspond to Applicants' linker sequence. Sufficient evidence of similarity is deemed to be present between the analogs of Konig et al and Applicants' claimed glycopeptides to shift the burden to Applicants to provide evidence that the claimed glycopeptides are unobviously different than the analogs of Konig et al.

11. Claims 1, 9-12, 14, 16-18, 22-25, 28-30, 32, and 34-37 are rejected under 35 U.S.C. 102(b) as being anticipated by Wagstaff et al (U.S. Patent No. 6,525,021). Wagstaff et al teach contulakin-G analogs, including analog A which comprises a glycosylated serine residue at position 10. The analogs are combined with pharmaceutically acceptable carriers and are used

pharmaceutically to provide analgesia and to treat, e.g., anxiety, depression, and Parkinson's disease. See, e.g., the Abstract; column 2, lines 10-25; column 14, lines 41-50; and Examples 4 and 7. The analogs of Wagstaff et al are amphipathic peptides because they comprises both hydrophilic (e.g., non-glycosylated Ser and Glu) and hydrophobic (e.g., Tyr, Ile, and Leu) amino acid residues. See Applicants' definition of "amphipathic" at page 6, last paragraph, lines 3-6. With respect to instant claims 9-11, 29, and 30, in view of the similarity in structure between the analogs of Wagstaff et al and Applicants' claimed glycopeptides, inherently the analogs of Wagstaff et al will adopt a helical conformation in the presence of a lipid bilayer, will be substantially non-helical in water in the absence of a lipid bilayer, will show a % helicity as measured by circular dichroism in water and in the presence of a lipid bilayer, and will cross the blood-brain barrier, to the same extent claimed by Applicants. Given the scope of potential message sequences, address sequences, and subjects embraced by Applicants' claims, inherently an N-terminal portion of the analogs of Wagstaff et al will function as a message sequence for at least one subject, inherently a C-terminal portion of the analogs of Wagstaff et al will function as an address sequence for at least one subject, and the remaining portion of the analogs of Wagstaff et al will correspond to Applicants' linker sequence. Sufficient evidence of similarity is deemed to be present between the analogs of Wagstaff et al and Applicants' claimed glycopeptides to shift the burden to Applicants to provide evidence that the claimed glycopeptides are unobviously different than the analogs of Wagstaff et al.

12. Claims 1, 22-27, and 32-34 are rejected under 35 U.S.C. 102(b) as being anticipated by Schambye et al (U.S. Patent Application Publication 2002/0127652). Schambye et al teach follicle stimulating hormone (FSH), comprising the α and β subunits. A nonapeptide comprising

two glycosylation sites is added to the N-terminus of the α-subunit. FSH comprises more than 19 amino acid residues. The modified FSH is combined with pharmaceutically acceptable carriers and excipients. See, e.g., Figure 1; paragraphs [0079] and [0200]; and Example 9. The modified FSH of Schambye et al is an amphipathic glycopeptide because it comprises both hydrophilic and hydrophobic amino acid residues. See Applicants' definition of "amphipathic" at page 6, last paragraph, lines 3-6. Given the scope of potential message sequences, address sequences, and subjects embraced by Applicants' claims, inherently an N-terminal portion of the modified FSH of Schambye et al will function as a message sequence for at least one subject, inherently a C-terminal portion of the modified FSH of Schambye et al will function as an address sequence for at least one subject, and the remaining portions of the modified FSH of Schambye et al will correspond to Applicants' linker sequence. Sufficient evidence of similarity is deemed to be present between the modified FSH of Schambye et al and Applicants' claimed glycopeptides to shift the burden to Applicants to provide evidence that the claimed glycopeptides are unobviously different than the modified FSH of Schambye et al.

13. Claims 1, 2, 7-14, 16-18, 20, 22-31, and 34-36 are rejected under 35 U.S.C. 102(b) as being anticipated by the Palian et al article (Peptides: The Wave of the Future, 2001, pages 499-501). The Palian et al article teaches amphipathic glycosylated enkephalins comprising an N-terminal opioid message sequence, a C-terminal address sequence, and a linker sequence Gly. The amphipathic glycosylated enkephalins are comprised of 17-20 amino acids, and one, two, or three of the serine residues present are β-glucosides. The amphipathic glycosylated enkephalins are largely unstructured in water and highly helical in the presence of micelles. The N-terminal opioid message sequences target the delta, kappa, or mu opioid receptors, and the amphipathic

glycosylated enkephalins provide good analgesia in vivo. See, e.g., Figures 1, 3, and 5; page 499, first and second paragraphs; and page 500, last paragraph. With respect to instant claim 8, "endorphin" is generic to enkephalins (see Applicants' specification at page 1, last paragraph, first line), and therefore the amphipathic glycosylated enkephalins of the Palian et al article also are glycosylated endorphins. Note also that the Palian et al article characterizes the amphipathic glycosylated enkephalins as "β-Endorphin Mimics" (see, e.g., the Title). With respect to instant claims 29 and 30, in view of the similarity in structure, amphipathicity, helicity, and analgesic activity between the amphipathic glycosylated enkephalins of the Palian et al article and Applicants' claimed glycopeptide, inherently the amphipathic glycosylated enkephalins of the Palian et al article will show a % helicity as measured by circular dichroism in water and in the presence of a lipid bilayer, and will cross the blood-brain barrier, to the same extent claimed by Applicants. Sufficient evidence of similarity is deemed to be present between the amphipathic glycosylated enkephalins of the Palian et al article and Applicants' claimed glycopeptides to shift the burden to Applicants to provide evidence that the claimed glycopeptides are unobviously different than the amphipathic glycosylated enkephalins of the Palian et al article.

14. Claims 1, 2, 6-12, 14, 16-18, 20, 22-26, 28-31, and 34-36 are rejected under 35 U.S.C. 102(a) as being anticipated by the Egleton et al article (Tetrahedron: Asymmetry, Vol. 16, pages 65-75). The Egleton et al article teaches helical endorphin-based glycopeptides 14-16 (see Table 3), which comprise an N-terminal delta-selective opioid message sequence YtGFL; a P, βA, or GG linker sequence; and a NLBEKALKS*L address sequence. The glycopeptides are 16 and 17 amino acids in length, and comprise a single serine glucoside residue. The glycopeptides are non-helical in water in the absence of a lipid bilayer, helical when bound to a micelle, and

transport across the BBB in mice. See also page 70, column 2, last full paragraph, through page 73, column 1, first full paragraph; and Figures 7 and 11. With respect to instant claim 29, in view of the similarity in structure, amphipathicity, helicity, and ability to cross the blood-brain barrier activity between the glycopeptides of the Egleton et al article and Applicants' claimed glycopeptide, inherently the glycopeptides of the Egleton et al article will show a % helicity as measured by circular dichroism in water and in the presence of a lipid bilayer to the same extent claimed by Applicants. Sufficient evidence of similarity is deemed to be present between the glycopeptides of the Egleton et al article and Applicants' claimed glycopeptides to shift the burden to Applicants to provide evidence that the claimed glycopeptides are unobviously different than the glycopeptides of the Egleton et al article.

Because the instant claims are not deemed to be entitled under 35 U.S.C. 119(e) to the benefit of the filing date of any of the provisional applications (see section above), and because the Egleton et al article is by others, the Egleton et al article is available as prior art against the instant claims under 35 U.S.C. 102(a).

15. The Polt et al article (Drugs of the Future, Vol. 26, pages 561-576) is cited as art of interest, being essentially duplicative of the references applied above.

16. The Information Disclosure Statement filed December 10, 2008 has not been considered by the examiner because a listing of the references was not provided as required by 37 CFR 1.98(a)(1).

17. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey E. Russel at telephone number (571) 272-0969. The examiner can normally be reached on Monday-Thursday from 8:00 A.M. to 5:30 P.M. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor Cecilia Tsang can be reached at (571) 272-0562. The fax number for formal communications to be entered into the record is (571) 273-8300; for informal communications such as proposed amendments, the fax number (571) 273-0969 can be used. The telephone number for the Technology Center 1600 receptionist is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Jeffrey E. Russel/
Primary Examiner, Art Unit 1654

JRussel
January 13, 2009